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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,626	12/09/2003	Tiina-Liisa Rasanen	LCTD-0035	4756

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 06/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,626	RASANEN ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *6-14 and 16-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants Response to Restriction Requirement Acknowledged

1. Applicants election with traverse the Group I invention along with 1-methylspermidine as the elected species, is acknowledged. Although applicant states that claims 1 to 7 and 15 read on the elected species, actually claims 1 to 5 and 15 read on the elected species. Claims 6 and 7 are drawn to optical isomers ((S)- and (R)-) of 1-methylspermidine.

Applicants traverse the restriction requirement on the grounds that there would be no burden in searching the entire groups. This argument is not persuasive, as claimed invention would be distinctive, each from the other for the reason of the record. Furthermore, the search of the entire groups in the non-patent literature (a significant part of a thorough examination) would be burdensome. Therefore, the requirement is still deemed proper, and made Final. Accordingly, claims 6-14 and 16-30 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claims.

2. With respect to the species election, it is noted that upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Information Disclosure Statement

3. Enclosed is an initialed copy of PTO 1449 filed April 25, 2006 which has been considered for your records. It is noted that the submitted IDS is identical to the IDS filed March 29, 2004.

Specification

4. The disclosure is objected to because they do not contain references to (i) Fig 1a, 1b, 1c and 1d, (ii) Fig. 3a, 3b, 3c and 3d, (iii) Fig. 4a, 4b, 4c and 4d, (iv) Fig. 5a and 5b, (v) Fig. 8a, 8b, 8c and 8d, and (vi) Fig. 9a and 9b in the Brief Description of the Drawing. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-5 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "treating pancreatitis" with a compound of formula (I), does not reasonably provide enablement for "preventing pancreatitis" or "a metabolically stable analogue of spermidine". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d

1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The instant claims are drawn to a method for treating or preventing pancreatitis comprising administering a compound of formula (I) or "a metabolically stable analogue of spermidine". The specification defines that "metabolic" refers to having to do with chemical changes involved in the processes of growth and repair in a living organism, including anabolic and catabolic changes.

Websters II Dictionary defines the term "prevent" as "anticipate or counter in advance, to keep from happening". The interpretation of the instant claims allows for the complete cure and eradication or total elimination of pancreatitis by the administration of said compounds.

With respect to the scope of enablement for "preventing pancreatitis",

It is known today that the pathophysiology of pancreatitis is still unclear for the most part, and there are still no causal therapeutic approaches or cure for pancreatitis available besides a purely symptomatic treatment of the disease ("Pancreatitis: Advances in Pathobiology, Diagnosis and Treatment", Barbu, S.T., Symposium Report, October 14-15, 2004; "Chronic Pancreatitis", www.patient.co.uk, 2004; "Hereditary Pancreatitis", www.pancreasfoundation.org,

2004). Thus, it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" or completely cure or eradication effect.

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmacy art is high. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the preventive utility of the instant compounds.

The specification provides the effects of methylspermidine or alpha-methylspermidein in reducing necrosis of pancreatic cells or the pancreatitis-associated edema in vivo (Examples 2, 5, 6, 12 and 13). However, there is no demonstrated correlation that the tests and results apply to the claimed preventive utility embraced by the instant claims.

Since the efficacy of the claimed compound(s) in preventing the pancreatitis mentioned above cannot be predicted from a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

With respect to enable of "a metabolically stable analogue of spermidine",

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584

F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5(BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotropic hormones was unpredictable art; In re Wright, 9999 F.2d 1577, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of treating or preventing pancreatitis prior to filling of the instant invention was an unpredictable art.

The claims are very broad due to the vast number of possible compounds of that are described as being "a metabolically stable analogue of spermidine". The instant claims cover "analogues of spermidine" that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

Although the specification discloses polyamine hydrocarbon compounds, preferably alkylated analogues of spermidine, as the suitable "metabolically stable analogues of spermidine", the specification fails to provide how to make/screen "metabolically stable analogues of spermidine" without undue amount of experimentation. As discussed in preceding comments, in the instant case, only a limited number of analogues that are structurally similar to

spermidine which is represented by the formula are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The instant claims read on any compounds having "a metabolically stable analogue of spermidine", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fishcher, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575.

As discussed above, considering above factors, especially the "sufficient working examples", "the level of skill in the art", "the relative skill and the unpredictability in the pharmaceutical art", "breadth of the claims" and "the chemical nature of the invention", one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the claimed compounds for the claimed methods of prevention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-5 and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Rasanen et al. (The Journal of Biological Chemistry, Vol. 277, No. 42, pp. 3867-39872, October 2002).

Rasanen teaches use of a polyamine analogue such as 1-mehtylspermidine for the treatment of pancreatitis (abstract, results and discussion).

7. Claims 1-5 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Jakus et al. (US 5344846).

Jakus teaches use of a deoxyhypusine synthase inhibitor such as polyamine including 1-methylspermidine (compound 35) for the treatment of mammalian cells to inhibit cell growth, especially for inhibiting the proliferative cell growth associated with malignant and non-malignant diseases (column 1, lines 14-62; Figure 4).

Although Jakus is silent about the prophylactic utility of said compound in preventing pancreatitis, such prophylactic utility deems to be inherent the referenced method. Applicant's attention is directed to Ex parte Novitski 126 USPQ 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a haec verba recitation for such prophylactic utility. In the instant case, as in Ex parte Novitski, the claims are directed to preventing a malady or disease

with old and well known compounds of compositions. The prior art administering compounds inherently possessing a protective utility anticipates claims directed to such protective use.

Conclusion

8. No Claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
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